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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,732	03/19/2001	David Mark Whitcombe	0380-P02328US	7974

110 7590 08/27/2002

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	19

DATE MAILED: 08/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/700,732	Applicant(s) Whitcombe
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Specification

1. Claims 1-14 have been amended

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6, 8-13, 15-20 , and 37 are rejected under 35 U.S.C. 102 (b) as being anticipated by Graham et al. (PCT International Publication Number WO 97/05280) (February 13, 1997).

Graham et al teach a method for determining the presence or absence of a target nucleic acid sequence in a sample nucleic acid (Abstract), the method comprising :

(a) exposing the sample to a detection agent comprising a metal surface associated with a SER(R)S active species (SAS) and with a target binding species (TBS) (Abstract, Claim 1, and page 16, The SER(R)S-active label Section to page 18, line 8),

(b) observing the sample/agent mixture using SER(R)s to detect any surface enhancement of the label, characterized in that the binding of the TBS to the target sequence causes increased surface enhancement of the SAS (Claim 1 and Figures 3-20).

Graham et al inherently teach a method, wherein the metal surface is not itself capable of surface enhancement when present in the detection agent of step (a) (page 23, The SER(R)S-active surface section, first paragraph).

Graham et al teach a method, wherein the detection agent is exposed to the sample in step (a) as two or more separate components (Abstract, Claim 1, and page 16, The SER(R)S-active label Section to page 18, line 8).

Graham et al teach a method, wherein the detection agent comprises a first agent and a second agent each having a different TBS, each TBS being capable of binding to the target sequence, and wherein the binding of the first and second TBS to the target sequence brings a metal surface associated with each TBS into proximity thereby causing surface enhancement of an SAS associated one or both of the metal surfaces (Table 1 and page 31, modification of the target or target binding species Section to page 35, third paragraph and page 26, last paragraph to page 27, second paragraph);

Graham et al teach a method, wherein the detection agent comprises monodisperse unaggregated colloidal metal particles associated with a TBS comprising a nucleic acid or nucleic acid analog which is complementary to all or part of the target sequence (Table 1, page 16, The SER(R)S-active label Section to page 18, line 8, page 24, second paragraph, and page 31, modification of the target or target binding species Section to page 35, third paragraph).

Graham et al teach a method, wherein the TBS comprises peptide nucleic acid (Page 35, third paragraph and page 39, last paragraph to page 40, line 4).

Graham et al inherently teach a method, wherein there are more than one TBS per metal colloid particle (Claim 2 and Table 1);

Graham et al teach a method, wherein a surface seeking group (SSG) is used to promote chemi-sorption of the SAS and /or TBS to the metal surface (page 40, chemi-sorptive functional group on the label subsection to page 44, line 5).

Graham et al teach a method, wherein the SSG is benzotriazole and azobenzotriazole and is modified with a dye which is SAS (Claims 16-19 and page 40, chemi-sorptive functional group on the label subsection to page 44, line 5).

Graham et al teach a method, wherein more than one target sequence is determined using multiple detection agents having distinguishable SAS (Page 61, last paragraph to page 62, first paragraph);

Graham et al teach a method, wherein

Graham et al teach a method, wherein the modified SSG is used to associate the TBS to the metal surface (page 40, chemi-sorptive functional group on the label subsection to page 44, line 5).

Graham et al teach a method, wherein the modified SSG is conjugated to the TBS via a linker group (Page 28, introduction of polyamine Section to page 34, third paragraph).

Graham et al inherently teach a method, wherein the target sequences share sequence identity, and wherein a common first agent is used in conjunction with specific distinguishable

second agents which can discriminate between the remainder of the target sequences (Abstract, and page 16, The SER(R)S-active label Section to page 18, line 8).

Graham et al teach a method for detecting the presence of, or selecting, or identifying, or phylogenetically classifying, an organism, the method comprising use of a method wherein the target nucleic acid sequence is associated with that organism (Uses of the Invention Section, page 59, last paragraph to page 64, second paragraph).

Graham et al teach a method for diagnosing a disease, the method comprising use of a method wherein the target nucleic acid sequence is associated with that disease (Uses of the Invention Section, page 60, last paragraph).

Graham et al teach a method for isolating a nucleic acid encoding a specific gene, the method comprising use of a method wherein the target sequence corresponds to a sequence associated with, or within, that gene (Uses of the Invention Section, page 59, last paragraph to page 64, second paragraph).

Graham et al teach a process for producing a detection agent, the process comprising the step of combining unaggregated metal particles with a SAS and a TBS, whereby the SAS and TBS associate with the metal particles via an SSG (Page 28, introduction of polyamine Section to page 34, third paragraph and page 40, chemi-sorptive functional group on the label subsection to page 44, line 5).

Graham et al teach a method, wherein the triazole group is a benzotriazole group (Page 41, line 1 to page 42, third paragraph).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 7 and 14 are rejected under 35 U.S.C. 103 (a) over Graham et al. (PCT International Publication Number WO 97/05280) (February 13, 1997).

Graham et al teach the method of claims 1-6, 8-13, 15-20, and 37 as described above.

Graham et al do not teach the method, wherein there are more than 1-20 TBS per metal colloidal particle and wherein the SAS is present in greater than 2-100 fold excess over the TBS.

However, it is *prima facie* obvious that selection of the specific number of TBS per metal colloidal particle and specific concentration ratio of SAS over the TBS represents routine

optimization with regard to production of desired binding complex and quantity as well as quality of nucleic acid analyte, which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific number of TBS per metal colloidal particle and specific concentration ratio of SAS over the TBS selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Response to Amendment

6. In response to amendment, all 112 (second paragraph) rejections are hereby withdrawn. However, all 102 (b) and 103(a) rejections are hereby maintained.

Response to Arguments

7. Applicant's arguments filed on July 30, 2002 have been fully considered but they are not persuasive.

Applicant argues that 102(b) rejection based on Graham reference should be withdrawn because Graham reference fail to show certain features of applicant's invention. In response to applicant's argument that the Graham reference fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., aggregation of colloidal SER(R)s surface is actually dependent on the presence of target sequence and the method is a "one pot" detection system) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that Graham reference does not teach the "metal surface" and "surface seeking groups capable of binding to metal surface" of the claimed invention. Applicant argues that the words "metal surface" and "surface seeking groups capable of binding to metal surface" was not found in Graham reference. Applicant argues that because Graham has a preferred embodiment of supports or beads, Graham is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Graham has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader

embodiments in the disclosure and that this does not constitute a teaching away. Graham reference uses metal (silver in this case) in the form of colloids to measure the presence of oligomers, and the property of "surface seeking groups capable of binding to metal surface" is inherently present in this chemically and structurally identical molecule (Example 5, Page 73, second paragraph). Graham teaches that such silver colloidal surfaces can be used to detect the nucleic acid by determining spectra (Page 68, third paragraph)). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, any metal and "surface seeking groups capable of binding to metal surface" under any suitable conditions can be used for detecting the presence or absence of a target nucleic acid.

In view of the response to arguments, all previous 102(b) and 103(a) rejection as well as lack of unity is hereby properly maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237

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Arun Chakrabarti,

Patent Examiner

August 15, 2002